UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/527,422 | 03/27/2006 | Birke Bartosch | P08575US00/BAS | 4780 |

881 7590 10/14/2010

STITES & HARBISON PLLC
1199 NORTH FAIRFAX STREET
SUITE 900
ALEXANDRIA, VA 22314

| EXAMINER | |
|---|---|
| POPA, ILEANA | |
| ART UNIT | PAPER NUMBER |
| 1633 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 10/14/2010 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

iplaw@stites.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/527,422 | BARTOSCH ET AL. | |
| | Examiner | Art Unit | |
| | ILEANA POPA | 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *03 August 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *46-91* is/are pending in the application.

4a) Of the above claim(s) *57,67,71-81 and 88-90* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46-56, 58-66, 68-70, 82-87 and 91* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

1 Claims 1-45 have been cancelled. Claims 57, 67, 71-81 and 88-90 have been withdrawn. Claims 46, 59, and 70 have been amended.

Claims 46-56, 58-66, 68-70, 82-87 and 91 are under examination.

***Response to Arguments***

***Claim Rejections - 35 USC § 103***

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 46-56, 58-66, 68-70, 82-87 and 91 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Marasco et al. (WO 00/55335), in view of both Lechmann et al. (Hepatology, 2001, 34: 4117-423) and Ray et al. (FEMS Microbiology Letters, 2001, 202: 149-156).

Marasco et al. teach an *ex vivo* method of producing infectious virus-like particles such as a flavivirus-like particle by **(i)** providing a packaging retroviral vector comprising a transgene and the cis-acting elements necessary for encapsidation, reverse transcription, and integration (i.e., a first nucleic acid sequence comprising a packaging competent retroviral genome), a vector encoding the retroviral gag-pol (i.e., a second vector comprising a cDNA encoding retroviral core proteins), and a vector encoding the

flavivirus envelope proteins (i.e., a third nucleic acid sequence comprising a cDNA encoding the envelope proteins), and **(ii)** transfecting host cells with the vectors above, culturing the transfected host cells to express the viral proteins and form the viral particles (claims 46, 48, 58, 70, and 84) (p. 4, third full paragraph, p. 6, first and second full paragraphs, p. 7, first paragraph, p. 16, p. 12, first and third paragraphs, p. 34, last paragraph, p. 41, third and fourth full paragraphs, claims 1-3 and 6-12). Marasco et al. also teach purifying their viral particles and using them to induce immune responses or to deliver transgenes to cells (claims 59, 82, and 83) (p. 34, last paragraph, p. 35). Although Marasco et al. teach their method as suitable to make infectious flavivirus-like particles, they do not specifically teach HCV, nor do they teach a HCV polyprotein comprising in order the core protein, the native E1 and E2 proteins, and the native p7 protein (claims 46-56, 58-66, 68-70, 82-87, and 91). Lechmann et al. teach obtaining infectious HCV-like particles wherein the HCV-like particles are made by using a vector encoding a polyprotein comprising successively the HCV core, E1, E2 and p7 proteins (Abstract, p. 417, column 2). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Marasco et al. by using the polyprotein of Lechmann et al. to achieve the predictable result of obtaining infectious HCV-like particles comprising functional hepacivirus glycoproteins assembled onto the retroviral core particles. By including HCV core protein, one of skill in the art would have necessarily included a signal sequence because the HCV core protein comprises a signal sequence, wherein the signal sequence is required for the proper polyprotein targeting to the host cell endoplasmic reticulum (see Ray et al., p. 150, column 1 and

Fig. 1). With respect to the limitation of a signal peptide derived from a type I membrane protein (claims 46 and 70), it is noted that the instant claim 70 defines that the signal sequence from a type I membrane protein could be the signal sequence from the core protein. Therefore, the combined teachings of Marasco et al. and Lechmann et al. disclose an infectious HCV-like particle obtained by using a nucleic acid sequence comprising a cDNA encoding a polyprotein containing successively a signal peptide from a type I protein, and the HCV E1, E2, and p7 proteins. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

The applicant argues that none of the cited documents teaches or suggests using E1 and E2 proteins comprising the transmembrane domains. In response, it is noted that the polyprotein of Lechmann et al. comprises the full E1 and E2 proteins (see paragraph bridging p. 417 and 418).

The applicant's arguments related to VSV pseudotyped viral particles are not new and were previously addressed. Specifically, the arguments are not material to the instant rejection because the instant rejection is based on producing HCV-like particles and not VSV pseudotyped viral particles. Producing HCV-like particles as taught by the combination of the art cited above requires the presence of the full length E1 and E2 proteins (i.e., including the transmembrane domain).

The applicant argues that the HCV-like particles described by Lechmann et al. are not particles wherein the HCV envelope proteins are assembled on a retroviral core. In response, it is noted that one cannot show nonobviousness by attacking references

individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The combination of Marasco et al. and Lechmann et al. teaches HCV-like particles wherein the HCV envelope proteins are assembled on a retroviral core and are thus similar to the instant particles and the particles described by De Beeck et al. and Sandrin et al.

***Conclusion***

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ileana Popa/
Primary Examiner, Art Unit 1633